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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,765	09/14/2006	Lisa Kadyk	05-1038-C5	3877

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
11/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,765	KADYK ET AL.	
	Examiner	Art Unit	
	JACOB CHEU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *20-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 9/9/2010 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

Claims 1-25 are pending.

Currently, claims 1-19 are under examination. Claims 20-25 are withdrawn from further consideration.

2. The objection on claims 1-19 are withdrawn due to amendment.

3. The rejections of claims 1-19 over 35 USC 112, first paragraph under enablement and written description are maintained as of record.

4. With respect to enablement rejection, the Remarks provides instructions and examples from the specification as to show one artisan in the field how Applicants reach to the conclusion as claimed invention, namely using the MELK peptides as a biomarker to screen potential compound(s) capable of modulating RAC pathway. The followings are excerpts from the Remarks:

The Office alleged that the claimed assays are not enabled because there is no data linking MELK with the RAC pathway and therefore further investigation is required to verify whether MELK is involved in the RAC pathway. Contrary to the Office's contention, the specification provides data linking MELK with the RAC pathway. Initially, the specification teaches that *ced-10, mig-2,* and *rac-2* encode RAC-related proteins and that these genes function to control a number

of cell and axonal migrations in *C.elegans*. The specification further teaches that inactivation of two or three of these genes causes significant migration defects, whereas mutation in only one of these genes does not. Specifically, the specification teaches that *ced-lOlmig-2* double mutants have gross morphological and movement defects not seen in either single mutant and that the phenotype of the *ced-lOlmig-2* double mutant includes slow growth, and

vulval, withered tail, and sterility defects, none of which is seen with either single mutant (specification at pages 1, and 34-35). Thus, *ced-lO* and *mig-2* single mutants resemble wildtype worms in morphology and movement, whereas *ced-lOlmig-2* double mutants have strong morphological and movement defects.

The link between MELK and the RAC pathway was determined using two separate assays involving *C.elegans* in which a specific gene was inactivated by RNAi. The assay methods and results are described in the specification at pages 4 and 34-35. Herein, the Applicants describe a first assay in which wildtype *C.elegans,* single *ced-lO* mutants, and single *mig-2* mutants, each having the same specific gene inactivated by RNAi were observed for morphological and movement defects resembling those of the *ced-lOlmig-2* double mutants.

Those genes that, when inactivated, result in a worm with a double *ced-lOlmig-2* mutant phenotype in the single *ced-lO* or single *mig-2* mutant *C.elegans* and not in the wildtype *C.elegans* were furthered studied in a second direct cell migration assay. The direct cell migration assay measures the migration of a subset of mechanosensory neurons (AVM and ALM) in *C.elegans* larvae. Those larvae having the *ced-lO/mig-2* double mutation show short or misguided AVM and ALM migration compared to wildtype larvae or larvae having the single *ced-lO* or single *mig-2* mutation.

compared with wildtype and single mutant *C.elegans)* are relevant to the RAC pathway. One such gene, 4B260, was identified. In other words, inactivation of 4B260 causes short or misguided cell migration in *C.elegans.* The human ortholog of the 4B260 gene is MELK.

One skilled in the art of genetic screening would understand that the two screening assays used and described in the specification are evidence of a link between MELK and the RAC pathway. Specifically, Applicants have shown that inactivation of 4B260/MELK by RNAi results in Rac-associated (i.e., ced-10 or mig-2 associated) changes in neuronal cell migration. Therefore, agents that modulate MELK (inhibit or enhance MELK) can be used to identify candidate RAC pathway modulating agents.

The Remarks have been considered but are not persuasive.

Examiner acknowledges using the insect model of ced-10/mig-2 for probing possible potential protein modulating agents. Using function recovery/loss by wild-type/mutant model is well-known and widely practiced in the field. However, the issue for enablement is the sole molecule identified in the specification, 4B260. As stated by Applicants, this molecule is a modifier of the RAC, albeit no data shown whether it is an enhancer or inhibitor. The specification further characterizes this molecule as followings:

"4B260 was an identified modifier from the screen. Orthologs of 4B260 are referred to herein as MELK.
BLAST analysis (Altschul et al., supra) was employed to identify orthologs of 4B260. For

example, representative sequence from MELK, GI #7661974 (SEQ ID NO:6), shares **38%** amino acid identity with the C. elegans 4B260." (see section 120 from PG-Pub)

By using BLAST analysis, Applicant asserts that there is a 38% homology between the 4B260 and the human MELK. The question boils down whether it is reasonable to one ordinary skill in the art, using this 38% homology peptide, to screen and identify any compound having the ability of modulating this 38% homology peptide and one artisan can reasonably connect this to the RAC pathway.

With such limited information, absence of identified conserved region(s) of interaction between the RAC and the 4B260, human MELK, one ordinary skill in the art would not jump to conclusion that any compound capable of modulating 4B260 is definitely involving in the RAC pathway since more experiments need to designed and conducted to further verify this conclusion. It is also reasonably conceivable that some compounds (capable of modulating 4B260) which fall outside the homology range, i.e. 62% diversity (not homologous with MELK), will be falsely identified as the potential modifiers. Taken together, with the insufficient disclosure to this 4B260, it would inevitably impose undue experiments to one ordinary skill in the art to further verify whether the identified compounds are in fact associated with RAC pathway.

5. With respect to the written description rejection, the Remarks reiterate the statement and experiments from the specification, Applicant concludes that they in fact possess the claimed invention.

The Remarks have been considered but are not persuasive.

The newly released "written description training guidelines" from this Office has a similar example illustrating the lack of written description in a claimed protein or fragment with functional activity (See claim 2 of Example 11A Percent Identity; http://www.uspto.gov/web/menu/written.pdf). In this example given by the Office, claim 2, "*an isolated nucleotide encoding the polypeptide with at least 85% sequence identity to SEQ ID No. 2, wherein the polypeptide has activity X*", is rejected mainly due to lack of disclosure on the correlation of structure and function on the protein. As discussed above, Applicant merely discloses a **38% homology** peptide to MELK (emphasis added). Similarly, there is no disclosure to the correlation of the function with any conserved domain(s) or region(s) on this peptide. In addition, no teaching or suggestion is revealed on the variations of deletion or addition on the protein that can be tolerated without losing the functional characteristics. Moreover, thus far

Applicant merely shows ONE species 4B260 (with mere 38% homology) for this MELK genus. It appears lacking a representative number of species justifying possession of whole genus. As in *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification needs "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. One cannot describe what one has not conceived.

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JACOB CHEU whose telephone number is (571)272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacob Cheu/
Primary Examiner, Art Unit 1641